REMARKS

These remarks are in response to the office action mailed December 18, 2002. Claims 17, 32-40 and 42-46 are currently pending. Applicants respectfully request reconsideration of the pending claims in view of the amendments and remarks provided herein.

A. Regarding the Amendment

By the present communication, claims 42 and 44-46 have been amended to more particularly define Applicants' invention. These amendments are supported by the specification and the original claims and add no new matter. Claim 42 has been amended merely to expressly recite the acronym "FP" as "fluorophosphonate." Support for this amendment can be found, for example, in the specification at page 62, paragraph 152. Claims 44-46 have been amended merely to recite by name the activity-based probes that were previously referred to by number. The amendments to these claims are set forth in the attached "Version With Markings To Show Changes Made" (Exhibit A).

B. Rejection Under 35 U.S.C. 112, first paragraph (new matter)

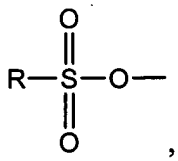
The rejection of claims 44-46 under 35 U.S.C. 112, first paragraph, as containing subject matter which was allegedly not described in the specification in such a way as to reasonably convey to those skilled in the art that the inventors, at the time the application was filed, had possession of the claimed invention, is respectfully traversed. Applicants respectfully disagree with the Examiner's assertion that the recitation of "sulfonate 1-sulfonate 17" in claims 44 and 46 have no support in the specification and claims as originally filed. Applicants submit that each sulfonate is expressly disclosed in the Figures and/or in the examples. For example, Figure 10 sets forth the chemical structures of sulfonates 1-11. In addition, paragraphs 202-218 describe a representative synthesis of invention sulfonates as well as characterization data for each sulfonate. Moreover, paragraph 225 further describes preparation of invention sulfonates (sulfonates 13 and 14), and paragraphs 235-238 further describes invention sulfonates 15-17. Thus, it is submitted that ample support for the recitation of "sulfonate 1-sulfonate 17" exists in the specification.

Nevertheless, to reduce the issues and expedite prosecution, the phrase "sulfonate 1-sulfonate 17" no longer appears in presently amended claims 44 and 46. Accordingly, it is respectfully submitted that this rejection is rendered moot.

B. Rejection Under 35 U.S.C. 112, first paragraph (written description)

The rejection of claims 42-46 under 35 U.S.C. 112, first paragraph, as containing subject matter which was allegedly not described in the specification in such a way as to reasonably convey to those skilled in the art that the inventors, at the time the application was filed, had possession of the claimed invention, is respectfully traversed. As a preliminary matter, Applicants note that although the rejection is set forth under 35 U.S.C. 112, first paragraph, it is asserted in the Office Action that claims 42-46 are allegedly "vague and indefinite." Thus, it is submitted that a rejection under 35 U.S.C. 112, second paragraph more accurately reflects the basis for the rejection. Regardless of the basis for the rejection, Applicants traverse for the following reasons.

With specific reference to claims 44 and 46, Applicants respectfully disagree with the Examiner's assertion that the term "Sulfonate 1" is unclear. The chemical structure of Sulfonate 1 is set forth in Figure 10, along with several other invention sulfonates. Indeed , those skilled in the art readily understand that, as used in the present specification "sulfonate" refers to the following chemical structure:



wherein R varies between the 17 sulfonates disclosed in the specification.

With specific reference to claim 45, Applicants respectfully disagree with the Examiner's assertion that the term "Sulfonate 15" is unclear. The specification (at paragraph 235) expressly describes sulfonate 15 as 2-pyridylsulfonyl octanoate, a variant of sulfonate 1.

With specific reference to the acronym "FP" as used in claim 42, this acronym is defined in the specification (see paragraph 152) as "fluorophosphonate". Thus, it is submitted that this acronym creates no ambiguity in claim 42.

Nevertheless, to reduce the issues and expedite prosecution, claim 42 has been amended to include the term "fluorophosphonate" and claims 44-46 have been amended to recite each activity-based probe specifically by name, rather than by number. Accordingly, it is respectfully submitted that this rejection is rendered moot.

C. **Rejections Under 35 U.S.C. 102**

The rejection of claims 17, 32-36, 38-40, 42, and 46 under 35 U.S.C. 102(b), as allegedly being anticipated by Liu, et. al. (*PNAS*, 1999, 96(26): 14694-14699), is respectively traversed. The filing date of the present application is December 15, 2000, which is less than one year after the publication date of Liu, i.e., December 21, 1999. Thus, it is submitted that Liu is not available prior art under 35 U.S.C. 102(b). Accordingly, reconsideration and withdrawal of the rejection of claims 17, 32-36, 38-40, 42, and 46 are respectfully requested.

The rejection of claims 17, 34, and 35 under 35 U.S.C. 102(b), as allegedly being anticipated by Zuk, et. al (U.S. Patent No. 4,281,061), is respectfully traversed. Applicants' invention, as defined by claim 17, distinguishes over Zuk by requiring a method for determining in a plurality of proteomic mixtures the presence of active target members of a group of related proteins in each of the proteomic mixtures, the related proteins related in having a common functionality for conjugation at an active site, comprising combining each of the proteomic mixtures with at least one activity-based probe comprising a reactive functionality specific for the active site when active, under conditions for conjugation of the probe(s) to the target members; determining the presence of target members conjugated with the probe in each of the proteomic mixtures; whereby the presence of the target members conjugated to the probe(s) in the proteomic mixtures is indicative of the presence of active target members in the mixtures.

Contrary to the Examiner's assertion, Zuk does not describe such a method. Instead, Zuk merely describes methods for determining trace amounts of organic compounds. Moreover, it is respectfully submitted that the methods described by Zuk could not be used to identify a group of related proteins in a proteomic mixture, since Zuk only describes the use of known polypeptides to identify trace amounts of small molecule organic compounds. Indeed, it is submitted that Zuk actually describes the opposite of the present invention, i.e, the use of known polypeptides to identify small organic molecules. In contrast, the present invention describes the use of activity-based-probes (ABPs) to identify groups of related proteins in a proteomic mixture.

Moreover, the Examiner has provided no objective evidence to support the assertion that a "labeled ligand" is equivalent to an activity-based probe, as this term is defined in the present specification. Indeed, the present methods, as defined for example by claim 17, require far more than merely "combining a sample with a labeled ligand." It is respectfully submitted that the assertion is merely conclusory and insufficient to form the basis of a rejection under 35 U.S.C. § 102(b). Accordingly, for all of the reasons set forth herein, reconsideration and withdrawal of the rejection are respectfully requested.

D. Rejection Under 35 U.S.C. § 103(a)

The rejection of claims 17 and 37 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Liu in view of Blanchard, et. al. (U.S. Patent No. 5,151,164), is respectfully traversed. As set forth above, Liu is not available as prior art. Thus, it is submitted that Liu can not be properly combined with another reference in a rejection under 35 U.S.C. § 103(a). Accordingly, withdrawal of this rejection is respectfully requested.

CONCLUSION

In view of the above amendments and remarks, reconsideration and favorable action on all claims are respectfully requested. In the event any matters remain to be resolved, the Examiner is requested to contact the undersigned at the telephone number given below so that a prompt disposition of this application can be achieved.

Please charge any additional fees, or make any credits, to Deposit Account No. 50-1355.

Respectfully submitted,

Date: March 18, 2003

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Enclosure: Exhibit A

Exhibit A

VERSION WITH MARKINGS TO SHOW CHANGES MADE

42. (Amended) A method according to any of Claims 11-13, 15-21, 32, 33, 35-38, 40 or 41 wherein said activity-based probe(s) are fluorophosphonate-biotin (FP-biotin).

44. (Amended) A method according to any of Claims 11-13, 15-20, 23, 24, 32, 33, 35-39 or 41 wherein said activity-based probe(s) are selected from the group consisting of [Sulfonate 1 – Sulfonate 17] 10-((2-pyridylsulfonyl)oxo)-N-biotinamidopentyldecanamide, 10-((Benzenesulfonyl)oxo)-*N*-biotinamidopentyldecanamide, 10-((*p*-Toluenesulfonyl)oxo)-*N*-biotinamidopentyldecanamide, 10-((4-Methoxybenzenesulfonyl)oxo)-*N*-biotinamidopentyldecanamide, 10-((Methylsulfonyl)oxo)-*N*-biotinamidopentyldecanamide, 10-((Butylsulfonyl)oxo)-*N*-biontinamidopentyldecanamide, 10-((Octylsulfonyl)oxo)-*N*-biotinamidopentyldecanamide, 10-((4-Nitrobenzenesulfonyl)oxo)-*N*-biotinamidopentyldecanamide, 10-((8-Quinolinesulfonyl)oxo)-*N*-biotinamidopentyldecanamide, 10-((2-Naphthalenesulfonyl)oxo)-*N*-biotinamidopentyldecanamide, 10-((2-Thiophenesulfony)oxo)-*N*-biotinamidopentyl)decanamide, α-undecylenyl alcohol, ((2-pyridylsulfonyl)oxo)-10-undecene, 10-((2-pyridylsulfonyl)oxo)-decanoic acid, 1-(2-pyridylsulfonyl)oxo-octane, 1-(2-pyridylsulfonyl)oxo-ethane, and 1-(methanesulfonyl)oxo-octane.

45. (Amended) A method according to claim 44 wherein said activity-based probe[(s) are Sulfonate 15] is 1-(2-pyridylsulfonyl)oxo-octane.

46. (Amended) A method according to Claim 14 or 34 wherein said activity-based probe(s) are selected from the group consisting of FP-biotin, FP-peg-biotin, [and Sulfonate 1-Sulfonate 17] 10-((2-pyridylsulfonyl)oxo)-N-biotinamidopentyldecanamide, 10-((Benzenesulfonyl)oxo)-*N*-biotinamidopentyldecanamide, 10-((*p*-Toluenesulfonyl)oxo)-*N*-

biotinamidopentyldecanamide, 10-((4-Methoxybenzenesulfonyl)oxo)-*N*-biotinamidopentyldecanamide, 10-((Methylsulfonyl)oxo)-*N*-biotinamidopentyldecanamide, 10-((Butylsulfonyl)oxo)-*N*-biontinamidopentyldecanamide, 10-((Octylsulfonyl)oxo)-*N*-biotinamidopentyldecanamide, 10-((4-Nitrobenzenesulfonyl)oxo)-*N*-biotinamidopentyldecanamide, 10-((8-Quinolinesulfonyl)oxo)-*N*-biotinamidopentyldecanamide, 10-((2-Naphthalenesulfonyl)oxo)-*N*-biotinamidopentyldecanamide, 10-((2-Thiophenesulfony)oxo)-*N*-biotinamidopentyl)decanamide, α-undecylenyl alcohol, ((2-pyridylsulfonyl)oxo)-10-undecene, 10-((2-pyridylsulfonyl)oxo)-decanoic acid, 1-(2-pyridylsulfonyl)oxo-octane, 1-(2-pyridylsulfonyl)oxo-ethane, and 1-(methanesulfonyl)oxo-octane.